

Appl. No. : 10/063,549  
Filed : May 2, 2002

### REMARKS

In response to the final Office Action mailed January 18, 2007, Applicants submit the foregoing amendments and following remarks. Claims 6, 8 and 10 have been amended; Claims 14-17 have been canceled. Claims 6-13 remain present for further examination.

#### **Rejections Withdrawn**

Applicants gratefully acknowledge the withdrawal of the rejections of the pending claims as lacking patentable utility and enablement. The PTO's reasons for withdrawal of the rejections include the following statement:

Applicant relies on more than 100 references, where expression levels of mRNA, measured by quantitative PCR, were found to have a good correlation to the expressed protein levels. ... While the PTO found several references in which the protein expression levels did not correlate with mRNA levels measured by quantitative PCR, the majority of the references which were found, including those cited by Applicant, demonstrated a correlation between mRNA levels measured by quantitative PCR and protein expression levels.

Applicant asserts that the expression levels of protein correlate to mRNA (cDNA) levels when the cDNA is measured by quantitative PCR (i.e. rt-PCR). Applicant has provided more than 100 references in support of this position. *Office Action* at 3-4 (emphasis added, citations omitted).

Applicants have submitted as exhibits numerous references in support of their assertion that, generally speaking, differential mRNA expression levels (e.g., tumor tissue vs. normal tissue) result in similar differential expression levels of the encoded protein. In addition, Applicants have submitted several Information Disclosure Statements listing numerous additional references, including those submitted as exhibits. Applicants have not represented to the PTO that all of the references submitted to the PTO in an IDS support Applicants' assertions.

Applicants have also argued that statements by the authors of Hu *et al.* (J. Proteome Res. 2003; 2(4):405-12) regarding the significance of differential mRNA expression detected by mRNA microarrays are not relevant to the data relied on by Applicants. Applicants' data in Example 18 of the instant application are based on rt-PCR, which is recognized by those of skill in the art as more sensitive and reliable than mRNA microarrays, and therefore the opinions of Hu regarding the significance of differential mRNA data from microarrays is not relevant to the instant application. Applicants' have not argued that microarray data are not reliable, or that all

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of the supporting references relied on by the Applicants' used quantitative rt-PCR to measure mRNA levels.

Finally, Applicants note for the record that they do not necessarily agree with the PTO's characterization of the references as set forth in the Office Action. Applicants do agree with the PTO's conclusion that "[b]ased on the totality of evidence of record, one of skill in the art would find it more likely than not that an increase in message as measured by rt-PCR would be predictive of an increase in protein expression levels, absence [*sic*] evidence to the contrary."

**Rejections Under 35 U.S.C. §112, first paragraph – Written Description**

Claims 14-17 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Solely to expedite allowance of the remaining claims, Claims 14-17 have been cancelled.

**Rejections Under 35 U.S.C. §112, Second Paragraph – Indefiniteness**

Claims 6, 8 and 12-17 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The PTO states that "the metes and bounds of the 'signal sequence' is *prima facie* indefinite and limitations from the specification or figure are not read into the claims." *Final Office Action* at 7.

The claims have been amended to recite the specific amino acid sequence of the signal peptide. Figure 46 of the specification as filed identifies particular portions of SEQ ID NO: 46, including the signal peptide sequence: amino acids 1-22. Thus, the amendment is fully supported by the application as filed, and the claims now specifically set forth "the metes and bounds of the 'signal sequence.'" Withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is therefore respectfully requested.

**Conclusion**

Applicants respectfully submit that claims are in condition for allowance. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: March 6, 2007

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